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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants	: Kenneth H. Grabstein et al.
Application No.	: 09/724,841
Filed	: November 28, 2000
For	: POLYNUCLEOTIDES ENCODING EPITHELIUM-DERIVED T-CELL FACTOR AND USES THEREOF
Examiner	: Prema Maria Mertz
Art Unit	: 1646
Docket No.	: 66033-10/2811-H
Date	: September 8, 2005

Attention: Board of Patent Appeals and Interferences
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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BOARD OF PATENT APPEALS
AND INTERFERENCES

APPELLANT'S BRIEF (37 C.F.R. § 41.37)

Commissioner for Patents:

Appellants appeal from the final rejection of claims 20-30, 34, 35 and 41-45 of the above-identified application. This Brief on Appeal is submitted in response to the Office Action of August 9, 2004, rejecting the claims. The appeal is proper because the claims have been rejected twice.

The fees required under Section 1.17(c), and a request for extension of time for filing this brief and fees therefor, are dealt with in the accompanying transmittal letter.

I. REAL PARTY IN INTEREST

The real party in interest in the above-identified application is Amgen Incorporated, a Delaware corporation, which has its principal place of business at One Amgen Center Drive, Thousand Oaks, CA 94608.

II. RELATED APPEAL AND INTERFERENCES

No other appeals or interferences will directly affect, be affected by, or have a bearing on the Board of Patent Appeals and Interferences' decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-19, 31-33, and 36-40 were previously cancelled. Claims 20-30, 34, 35 and 41-45 stand rejected and are the claims on appeal. No other claims are pending.

IV. STATUS OF AMENDMENTS

In a Response filed on June 29, 2004, Appellants amended claims 20, 28 and 34. The claims as shown in the accompanying Appendix are an accurate representation of the pending claims. The status of the prior amendments is relevant to the analysis of the current grounds of rejection on appeal, and is therefore summarized below for the Board's convenience.

Office Action mailed January 8, 2003. The Examiner stated that claims 20-30 were allowable if the pending rejections were overcome, and no prior art rejections were made.

Appellants' response mailed April 3, 2003. Claims 20-25 were amended to be free of the language objected to by the Examiner.

Office Action mailed June 12, 2003. The Examiner indicated that the rejection of claims 20-30 under 35 U.S.C. § 112, first paragraph, and of claims 20-25 under 35 U.S.C. § 112, second paragraph (in reference to "consisting essentially of") were withdrawn. Other rejections based on specific claim language were maintained, and the action was made final.

Amendment after final filed on December 1, 2003. The claim language was amended to address the remaining grounds of rejection.

Advisory Action mailed December 24, 2003. The Examiner stated that claims 20-30 were allowed. Claims 36-40 were rejected in view of the "moderate stringency" language. Therefore based on the status of the case as of December 24, 2003, Appellants reasonably believed that by canceling claims 36-40, claims 20-30 could proceed to issue.

Request for Continued Examination (RCE) filed on February 5, 2004. This RCE was filed just six weeks after Appellants received notice that claims 20-30 were allowed. Claims 36-40, the only previously rejected claims, were canceled by amendment.

Office Action mailed March 31, 2004. Despite being allowed just three months earlier, claims 20-30 were rejected on numerous grounds, including 35 U.S.C. § 112,

first paragraph (written description); 35 U.S.C. § 112, second paragraph (indefiniteness), and for the first time, 35 U.S.C. § 102(b) over a prior art reference, with no indication why the reference published in 1991 was not cited in the parent application.

Response filed June 30, 2004. Appellants filed a response to address all these issues, by argument and amendment. Appellants further amended the claims using language suggested by the Examiner in the March 31, 2004 Office Action. In this response, Appellants also summarized the prosecution history, with a discussion of the previous allowance of claims 20-30.

Office Action (Final) mailed August 9, 2004. The Action contained new (despite the finality) 35 U.S.C. § 112, first paragraph, rejections, and the previous rejections were maintained.

Response filed on December 8, 2004. Arguments and amendments were filed to address the new and previous grounds of rejection.

Advisory Action mailed December 21, 2004. The Examiner did not enter the amendment, solely on the grounds that an amendment (with an obvious typographical error, SEQ ID NO:12 instead of SEQ ID NO:13, that the Examiner should have recognized) to overcome the prior art raised an issue of new matter.

Summarizing this extensive history of claim amendments, Appellants submit that the Examiner erred when she failed to abide by her previous indication that claims 20-30 were allowable, and failed to allow the case to go to issue when Appellants canceled all the remaining rejected claims on February 5, 2004. It is unclear why claims 20-30, which were allowed on December 24, 2003, became subject to numerous grounds of rejection just three months later. No reason was given that would justify this, such as a relevant change in the law.

Meanwhile, the Court of Appeals for the Federal Circuit has now issued clear guidelines for evaluating written description in the area of polynucleotide claims. In *Capon v. Eshhar,* Slip. Op. 03-1480, -1481 (Fed. Cir. August 12, 2005), case law that this Examiner previously cited in the Office Action dated August 9, 2004, was found not to be controlling precedent under facts that, as argued below, Appellants believe are analogous to the present claims.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to a mammalian epithelium-derived T-cell factor, now referred to as IL-15. Appellants discovered and sequenced a nucleic acid that encodes IL-15, and also prepared polypeptides that stimulate proliferation and differentiation of T-lymphocytes.

As described in the specification, one use of the protein is to promote long-term *in vitro* culture of T-lymphocytes and T-cell lines. (Page 6, lines 5-8.) In particular, purified protein (referred to as rETF, for recombinant Epithelium-Derived T-cell Factor) stimulated *in vitro* proliferation of CTLL-2 cells. (Example 6, page 40, lines 1-17.) The protein also induced cytotoxic T-lymphocyte lytic activity, lymphokine activated killer cell activity, and natural killer cell activity in human peripheral blood mononuclear cells.

These activities have important ramifications for treating diseases that involve T-cell activity. For example, natural killer T-cells play a role in destroying tumor cells and virus-infected cells in the body. Using the protein of the invention to stimulate T-cells will expand the population of cells that destroy tumor cells and will also be instrumental in destroying virus-infected cells. (Page 45, lines 6-15.) Independent claim 20 is supported at page 26, lines 27-34 and page 3, lines 16-23, and recites an isolated nucleic acid of at least 12 contiguous nucleotides in length selected from the group consisting of (a) a nucleic acid consisting of SEQ ID NO:1; (b) a nucleic acid consisting of SEQ ID NO:4; (c) a nucleic acid complementary to SEQ ID NO:1, and (d) a nucleic acid complementary to SEQ ID NO:4 wherein said isolated nucleic acid of (a), (b), (c), or (d) is capable of specifically binding to the complement of the polynucleotide of SEQ ID NO:1; the complement of the polynucleotide of SEQ ID NO:4; SEQ ID NO:1; or SEQ ID NO:4, respectively.

The claims on appeal relate to several aspects of the invention. Dependent claims 21-30, 34 and 35 provide isolated polynucleotides of various lengths having contiguous nucleotides from polynucleotides of the invention. In certain embodiments, the polynucleotide is claimed as part of a composition (claim 30). In other embodiments (claim 34) the nucleic acid is DNA or RNA. Claims 20-30, 34 and 35 all refer to polynucleotide aspects of the invention, meaning material that either encodes IL-15, or can be used as a probe to detect a polynucleotide encoding IL-15. These embodiments

are described throughout the specification, particularly at page 26, lines 19-36 and page 27, lines 1-8 and 24-30.

Independent claim 41 recites an oligonucleotide of at least 14 nucleotides in length capable of hybridizing to a nucleic acid which encodes a polypeptide of SEQ ID NO:3 or SEQ ID NO:6. The dependent claims, 42-44, relate to the invention as described at page 12, lines 14-22, and recite oligonucleotides of at least 14 nucleotides in length capable of binding to mRNA encoding IL-15, or to the related cDNA sequences. Dependent claim 45 represents a particular embodiment in which the oligonucleotide is part of a composition also comprising a pharmaceutically acceptable diluent or carrier.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Did the Examiner err by rejecting claims 20-25 under 35 U.S.C. § 112, first paragraph, for alleged failure to comply with the written description requirement, because the recitation of "at least 12 nucleotides" is not new matter?

II. Did the Examiner err by rejecting claims 20-30, 34, 35, and 41-45 under 35 U.S.C. § 112, first paragraph, for lack of enablement, because one of skill in the art is enabled to make and use the invention?

III. Did the Examiner err by rejecting claims 41-45 under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement, because the specification does provide an adequate written description of a DNA?

IV. Did the Examiner err by rejecting claims 41-45 under 35 U.S.C. § 112, second paragraph, for indefiniteness, because the specification does adequately define stringency conditions?

V. Did the Examiner err by rejecting claims 20-22, 26-27, 34, 35 and 41-45 under 35 U.S.C. § 102(b) as being anticipated by Smith *et al.*, because claims 41-45 recite sequences that are longer than the Smith *et al.* sequence, and because limitations in independent claim 20 place it and the remaining dependent claims beyond the scope of this rejection?

VII. ARGUMENTS

I. Did the Examiner err by rejecting claims 20-25 under 35 U.S.C. § 112, first paragraph, for alleged failure to comply with the written description requirement, because the recitation of "at least 12 nucleotides" is not new matter?

The Examiner stated that "at least 12 contiguous nucleotides" is new matter in claim 20. Appellants first wish to note that the intent of the written description requirements is to ensure that claims have written support in an earlier application on which Appellants rely for priority, not written support in the same application in which they are pending. See, for example, *In re Kraslow*, 707 F. 2d 1366, 1375. The specification supports the embodiment of "at least 12 contiguous nucleotides," for example, at page 26, lines 25-32: "as few as about 12 nucleotides in length, usually about 14 to 18 nucleotides in length . . . ." Clearly, "as few as" is equivalent to "at least" in that both designate a lower limit of 12 and an upper limit further specified as appropriate.

The goal of the written description requirement is to prevent a patent applicant from claiming priority to earlier applications if the current application discloses new matter not present in the earlier applications (*Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Further, *In re Kaslow* affirms that "the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language" (707 F.2d 1366, 1375 (Fed. Cir. 1983)).

Appellants submit that the Examiner misapplied the written description requirement in this case. While the current application is a continuation of an earlier application, the claimed subject matter is fully supported by the specification of the current application, including the phrase "at least 12 nucleotides." Furthermore, Appellants' position is supported by the recent Federal Circuit decision on the written description requirement, *Capon v. Eshhar*, Slip Op. 03-1480, -1481 (Fed. Cir., August 12, 2005). The parties in *Capon* argued that "precedent does not establish a *per se* rule requiring nucleotide-by-nucleotide re-analysis when the structure of the

component DNA segments is already known, or readily determined by known procedures." (Slip Op. at 12.) The Court agreed, and noted that the Board erred in refusing to consider the state of the scientific knowledge. (Slip Op. at 14.)

Appellants submit that the state of the scientific knowledge for the present claims mandates a finding that the term "as few as about 12 nucleotides in length, usually about 14 to 18 nucleotides in length," in reference to a polynucleotide sequence provided in the specification (SEQ ID NO:1), would be understood by one of skill to also mean "at least 12 contiguous nucleotides." This situation is, by analogy, clearly within that of *Capon v. Eshhar*, wherein the written description requirement does not require "a re-description of what was already known." (Slip Op. at 14.)

II. Did the Examiner err by rejecting claims 20-30, 34, 35, and 41-45 under 35 U.S.C. § 112, first paragraph, for lack of enablement, because one of skill in the art is enabled to make and use the invention?

The Examiner stated that Appellants have not taught how to further modify a nucleic acid molecule such that it binds to its target, and cited *In re Hutchison*, 69 U.S.P.Q. 138 (C.C. P.A. 1946). Appellants submit that *Hutchison* fails to support the position that the term "capable of" is not a positive limitation. Although claims 42 and 58 in *Hutchison* recite "capable of" language, they also recite "adapted" language, which is construed by the Court. However, the Court does not appear to focus on or interpret the specific phrase "capable of" anywhere in the opinion. Appellants submit that the Examiner failed to point out the language in *Hutchison* that interprets "capable of," as distinguished from interpretation of other claim language at issue in that case (and not present in Appellants' pending claims).

Furthermore, "capable of" is a widely used and accepted term in claim language. With examples too numerous to list here, a brief search of the U.S.P.T.O. database yielded 900 patents with the terms "capable of" and "polynucleotides" in the claims and 531 patents with the exact term "capable of hybridizing" in the claims. Thus, there is overwhelming precedent for such claim language, and the concept of "further modifying" a nucleic acid molecule so that it can bind to its target is not relevant. The "capable of" language refers to an intrinsic property already possessed by the claimed nucleic acid molecule.

III. Did the Examiner err by rejecting claims 41-45 under 35 U.S.C. § 112, first paragraph, for failure to comply with the written description requirement, because the specification does provide an adequate written description of a DNA?

As discussed above, the written description requirement was not designed to ensure an exact match of wording between an application and claims supported in that same application; instead, it related to ensuring claim support in a previous application. However, in an effort to advance the prosecution of this application, Appellants previously sought to amend claim 41 to recite conditions of high stringency for hybridization, as supported in the specification at, for example, page 26, line 24. However, this amendment was not entered, for unrelated reasons.

Although the amendment Appellants submitted has not been entered, the grounds for non-entry were not related to this rejection, and Appellants respectfully request that the Board take into consideration Appellants' previous attempt to address this ground of rejection.

IV. Did the Examiner err by rejecting claims 41-45 under 35 U.S.C. § 112, second paragraph, for indefiniteness, because the specification does provide an adequate definition of stringency conditions?

Appellants previously sought to amend claim 41 to recite that the oligonucleotide specifically hybridizes to the recited nucleic acid. This is supported in the specification, for example, at page 27, lines 25-29 ("sequences which are highly specific and form stable duplexes with the target sequence"; "should not form . . . duplexes with other regions of DNA."). The amendment was not entered, for unrelated reasons. Appellants respectfully request that the Board take into consideration Appellants' previous attempt to address this ground of rejection.

V. Did the Examiner err by rejecting claims 20-22, 26-27, 34, 35 and 41-45 under 35 U.S.C. § 102(b) as being anticipated by Smith *et al.*, because claims 41-45 recite sequences that are longer than the Smith et al. sequence, and because limitations in dependent claim 20 place it and the remaining dependent claims beyond the scope of this rejection?

In this instance, the oligonucleotide of Smith *et al.* comprising the sequence ATGAGAATTTCGA would not specifically bind to a polynucleotide bound by the nucleic

acids recited in claim 20, and would be outside the scope of the claims. Appellants therefore sought to amend claim 20 to recite "at least 14 contiguous nucleotides" and to add the proviso that the claimed nucleic acid is not ATGAGAATTTCGA. Appellants submit that this amendment, which was not entered based on the Examiner's conclusion that it is new matter (Advisory Action, December 21, 2005), does not raise an issue of new matter, because under the written description guidelines of *Capon v. Esshar* as discussed in Section I above, the claims need not re-describe what is already know.

Respectfully submitted,
Kenneth H. Grabstein et al.
DAVIS WRIGHT TREMAINE LLP

By _____
Kerry Fluhr
Registration No. 51,686

Enclosures:
Postcard
Form PTO/SB21
Petition for an Extension of Time and Fee Transmittal (+1 Copy)
Two copies of this Brief

2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Phone: (206) 903-3932
Facsimile: (206) 628-7699

VIII. APPENDIX OF CLAIMS INVOLVED IN THE APPEAL

20. An isolated nucleic acid of at least 12 contiguous nucleotides in length selected from the group consisting of (a) a nucleic acid consisting of SEQ ID NO:1; (b) a nucleic acid consisting of SEQ ID NO:4; (c) a nucleic acid complementary to SEQ ID NO:1, and (d) a nucleic acid complementary to SEQ ID NO:4 wherein said isolated nucleic acid of (a), (b), (c), or (d) is capable of specifically binding to the complement of the polynucleotide of SEQ ID NO:1; the complement of the polynucleotide of SEQ ID NO:4; SEQ ID NO:1; or SEQ ID NO:4, respectively.

21. The nucleic acid of claim 20 which is 12 to about 75 contiguous nucleotides in length.

22. The nucleic acid of claim 20 which is 12 to 14 nucleotides in length.

23. The nucleic acid of claim 20 which is 14 to 18 nucleotides in length.

24. The nucleic acid of claim 20 which is 18 to 20 nucleotides in length.

25. The nucleic acid of claim 20 which is 20 to about 75 nucleotides in length.

26. The nucleic acid of claim 20 labeled with a radioactive, fluorescent, enzymatic, or chromogenic marker.

27. The nucleic acid of claim 20 wherein the nucleic acid is DNA.

28. The nucleic acid of claim 27 selected from the group consisting of (a) a nucleic acid consisting of SEQ ID NO:9; (b) a nucleic acid consisting of SEQ ID NO:10; (c) a nucleic acid consisting of SEQ ID NO:11; (d) a nucleic acid complementary to SEQ ID NO:9; (e) a nucleic acid complementary to SEQ ID NO:10; and (f) a nucleic acid complementary to SEQ ID NO:11.

29. The nucleic acid of claim 27 selected from the group consisting of SEQ ID NO:9, SEQ ID NO:10, and SEQ ID NO:11.

30. A composition comprising the nucleic acid of claim 20 and a diluent or carrier.

34. The nucleic acid of claim 20 wherein the nucleic acid is DNA, or RNA.

35. The nucleic acid of claim 20 where the nucleic is RNA.

41. An oligonucleotide of at least 14 nucleotides in length capable of hybridizing, under conditions of moderate stringency, to a nucleic acid which encodes a polypeptide comprising SEQ ID NO:3 or SEQ ID NO:6.

42. The oligonucleotide of claim 41 which is DNA or RNA.

43. The oligonucleotide of claim 41 which is DNA.

44. The oligonucleotide of claim 41 which is RNA.

45. A composition comprising the oligonucleotide of claim 41 and a pharmaceutically acceptable diluent or carrier.